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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,441	08/05/2003	Boris Skurkovich	53663-5007-02	8293

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EXAMINER
DEVI, SARVAMANGALA J N

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/634,441	SKURKOVICH ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *11-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11606, 71706, 42608*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election

1) Acknowledgment is made of Applicants' election filed 11/06/06 in response to the species election requirement mailed 07/10/06. Applicants have elected the composition species comprising an antibody to tumor necrosis factor alpha, i.e., claims 1-10. Because Applicants did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P § 818.03(a)).

Status of Claims

2) Claims 1-20 are pending.

Claims 11-20 have been withdrawn from consideration as being not directed to a elected invention or species. See 37 C.F.R 1.142(b) and M.P.E.P § 821.03.

Claims 1-10 are under examination.

Information Disclosure Statements

3) Acknowledgment is made of Applicants' information disclosure statements filed 11/06/06, 07/17/06, and 04/26/04. Except for the citations of non-submitted books, the information referred to therein has been considered and a signed copy is attached to this Office Action.

Priority

4) This application is a continuation-in-part of the application 09/894,644, filed 02/21/2003, *now pending*, which is a continuation of application 09/894,287, filed 06/28/2001, now US patent 6,534,059, which claims domestic priority to the U.S. provisional application 60/295,895, filed 06/05/2001.

Specification

5) The specification is objected to for the following reasons:

(a) The use of the trademarks has been noted in this application. For example, see 'Sepharose' on page 10. Each letter of the trademark must be capitalized. See M.P.E.P 608.01(V) and Appendix l. Although the use of trademarks is permissible in patent applications, the propriety nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks. It is suggested that Applicants

examine the whole specification and make necessary changes wherever trademark recitations appear.

(b) On page 8, line 17, the address of the American Type Culture Collection is incomplete. Effective 23 March 1998, ATCC has a new address: 10801 University Boulevard, Manassas, VA 20110-2209. Amendment to the specification is suggested to reflect this. It is suggested that Applicant examine the whole specification to make similar correction to the address, wherever it appears.

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

6) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

7) Claim 9 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Claim 9 is indefinite, confusing, and has improper antecedence in the limitation: 'The heavy chain antibody of claim 8'. Claim 9 depends from claim 8, which is not drawn to a heavy chain antibody.

Rejection(s) under 35 U.S.C. § 103

8) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

9) Claims 1-7 and 10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Jonker *et al.* (WO 90/10707 – Applicants' IDS) in view of Pluenneke (US 2001/0021380 A1).

The transitional limitations 'having', 'comprising', 'including', 'containing' or 'characterized by', represent open-ended claim language and therefore, do not exclude additional, unrecited elements. See MPEP 2111.03 [R-1]. See *Moleculon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986)*; *In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('comprising' leaves 'the claim open for the inclusion of unspecified ingredients even in major amounts'). Therefore, the limitation 'comprising' in the instant claim(s) allows additional elements to be present in the recited composition. It should be noted that the transitional phrase 'consisting of' excludes any element, step, or ingredient not specified in the claim. *In re Gray, 53 F.2d 520, 11 USPQ 255 (CCPA 1931)*; *Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948)* ('consisting of' defined as 'closing the claim to the inclusion of materials other than those recited except for impurities ordinarily associated therewith.').

Jonker *et al.* disclosed a method of treating an immunoregulatory disorder, including an organ or tissue transplant rejection, by co-administering to a mammal, preferably a human, an effective amount of a composition comprising a pharmaceutically acceptable carrier and an antibody to tumor necrosis factor alpha. The antibody is specific to human TNF alpha, and is suitable for administration to the human body. The antibody is of human origin and can be a recombinant antibody, monoclonal or polyclonal antibody, IgG, or Fv, F(ab')2 or Fab fragment. The recombinant antibody is derived from a murine antibody wherein hypervariable or complementarity determining regions have been grafted into the variable framework regions of a human antibody. The antibody is administered parenterally or topically. See abstract; claims 6, 9 and 10; and pages 3-7. While Jonker's method, illustrated by way of example only, includes a method of treating skin graft rejection, Jonker's disclosure does not exclude, but includes within the scope of the disclosed 'immunoregulatory disorder', a method of treating other organ transplant rejections.

The teachings of Jonker *et al.* are explained above which do not expressly disclose the use of their method in the treatment of corneal transplant rejection.

However, Pluenneke expressly disclosed that anti-TNF alpha antibodies are used to treat or

prevent corneal transplant rejection. See section [0071].

Given Pluenneke's explicit teaching that anti-TNF alpha antibodies are used to treat or prevent corneal transplant rejection, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use or extend Jonker's method of treatment of organ transplant rejection by topical administration of a composition comprising anti-TNF alpha antibodies to treat another organ transplant rejection such as corneal transplant rejection in humans to produce the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of also treating, advantageously, transplant rejection of another organ other than skin, such as the corneal transplant rejection taught by Pluenneke in addition to the rejection of skin transplants. That the topical administration of a composition comprising an anti-TNF alpha antibody in humans to treat corneal transplant rejection includes topical administration to an eye having corneal transplant is impliedly taught by the combined teachings of the prior art references.

Claims 1-7 and 10 are *prima facie* obvious over the prior art of record.

10) Claim 8 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Jonker *et al.* (WO 90/10707 – Applicants' IDS) as modified by Pluenneke (US 2001/0021380 A1) as applied to claim 1, and further in view of Skurkovich *et al.* (*Curr. Opin. Mol. Therap.* 15: 52-57, February 2003) (Skurkovich *et al.*, 2003) and Spinelli *et al.* (*Nature Struct. Biol.* 3: 752-757, September 1996).

The teachings of Jonker *et al.* as modified by Pluenneke are explained above, which do not disclose that the antibody used in the method is a heavy chain antibody.

However, the use of camelid (i.e., heavy chain) antibodies was already suggested in the art for the treatment of autoimmune diseases including transplant rejection. For instance, Skurkovich *et al.* (2003) suggested the use of camelid antibodies in the treatment of autoimmune diseases including transplant rejection. Skurkovich *et al.* (2003) taught that camelid antibodies are closely homologous to human antibodies (see abstract; title; Table 1; and second full paragraph on page 56).

Spinelli *et al.* taught the advantages of using camelid antibodies by teaching that the camelid antibodies are devoid of a light chain and that they constitute a potentially valuable tool for applications in biotechnology. Spinelli *et al.* taught that immunization of camels or llamas

provides a way of obtaining recombinant heavy-chain variable fragments, which are produced as highly soluble monomers in heterologous organisms (see page 752).

Given Skurkovich's (2003) express suggestion to use heavy chain camelid antibodies in the treatment of transplant rejection, and given Spinelli's teaching that camelid antibodies devoid of light chains constitute a potentially valuable tool for applications in biotechnology, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to replace the human antibody in Jonker's method as modified by Pluenneke with the heavy chain camelid antibody of same specificity by making such antibodies recombinantly as taught by Spinelli *et al.* to produce the method of the instant invention with a reasonable expectation of success. One of skill in the art would have been motivated to produce the instant invention for the expected benefit of providing antibodies of an alternative source, which antibodies are known in the art to be closely homologous to human antibodies as taught by Skurkovich *et al.* (2003) and which antibodies are produced recombinantly in a highly soluble form as taught by Spinelli *et al.*

Claim 8 is *prima facie* obvious over the prior art of record.

Remarks

11) Claims 1-10 stand rejected.

12) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax number (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

13) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

14) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

15) Any inquiry concerning this communication or earlier communication(s) from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail service. The Examiner can normally be reached on Monday to Friday from 7.15 a.m to 4.15 p.m. except one day each bi-week which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Jeffrey Siew, can be reached on (571) 272-0787.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

November, 2006

S. DEVI, PH.D.
PRIMARY EXAMINER